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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,821	11/13/2000	Todd M. Kinsella	A-70036/RMS/JJD	9149

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,821	KINSELLA, TODD M.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-13 and 15-45* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15-17,19-25,28,30-32 and 38* is/are rejected.

7)☒ Claim(s) *18, 26-27, 29, 33-37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and response filed on 5/12/05 has been fully considered and entered into the application.

2. Claims 7-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/26/03.

3. This application contains claims 7-12 are drawn to an invention nonelected with traverse in Paper filed on 9/26/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. Claims 7-13, 15-45 are currently pending in this application, and claims 13, 15-45 are currently being examined in this application.

Priority

5. This application claims priority to provisional application 60/165,189 filed on 11/12/99.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The instant Patent application (09/712,821) specification is not same as the priority provisional application specification. For example the provisional application specification has not disclosed the instantly claimed expression vector combination. The provisional application

has not disclosed expression vectors with HBEGF. Further the newly incorporated subject matter of US Patent application 09/710,058 was not present in the provisional application specification. Thus, the instantly claimed invention gets the effective filing date of the instant application filing date 11/13/00.

6. Applicant's response filed on 5/12/05 does not address the priority claim. Thus, the effective filing date of the instant application is considered as the filing date of the instant application 11/13/00.

Drawings

7. The drawings filed on 5/12/05 have been considered and placed in the application.

Claim Objections

8. The objection to claim 30 set forth in the previous office action has been withdrawn in view of the amendment filed on 5/12/05.

Withdrawn Claim Rejections

9. The new matter rejection of claims 25-37 has been withdrawn in view of applicant's response.

10. The lack of antecedent basis rejections of claims 21 and 38, have been withdrawn in view of the amendments to the claims.

11. The written description rejection set forth in the previous office action has been withdrawn in view of the amendment and applicants response filed on 5/12/05.

Maintained Claim Rejections

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The obviousness rejection of claims 13, 15-17, 19-20, 30, 32 over US patent 6,465,253 B1 (Wickham et al) and US patent 6,613,563 B1 (Sosnowski et al) has been maintained for the reasons of record.

New Claim Rejections Necessitated by the Amendment

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 21-24, 38-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the limitation "the first and second selection genes" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claim 32 is dependent claim 31, and claim 31 recites the additional selection gene is GFP. However claim 32 recites that eh additional selection gene is drug resistance gene, which is different from claim 31 limitations. Applicants are requested to amend the claim to clarify the claimed subject matter in claim 32.

Claim 38 recites the limitation "the first and second selection genes" in line 4. There is insufficient antecedent basis for this limitation in the claim.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 15, 16, 17, 19, 20, 30, 32 and amended claims 25, 28, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,465,253 B1 (Wickham et al) and US patent 6,613,563 B1 (Sosnowski et al).

The instant claims recite an expression vector comprising a nucleic acid encoding HBEGF, GFP and IRES and a promoter.

NOTE that the instant amended claims recite 'a promoter of interest.'

Wickham et al teach vectors and methods for gene transfer to cells. The reference teaches modified adenovirus vectors comprising non-native amino acid sequences. The reference teaches non-native amino acid sequence of UTV or Universal Transfer Vector sequences. The reference preferably teaches the non-native amino acid sequence or UTV sequence comprises heparin binding motifs, and a stretch of 21 amino acids of the heparin binding epidermal growth factor like growth factor (HB-EGF) (refers to the HBEGF of the instant claims). The reference teaches adenoviral vectors, which can comprise additional sequences, a protease recognition sequence (refers to 2a site of the instant claims) (e.g., see column 17). The reference teaches that the vectors comprise additional marker genes such as gene encoding GFP (refers to the second

selection gene or GFP of the instant claims) (e.g., see column 19). The reference teaches that the non-coding sequences include promoter sequences. Wikham et al teach that the expression vectors comprise a promoter which operably linked to the coding sequences (i.e., see columns 15, 16).

The claimed invention differs from the prior art teachings by reciting that the expression vector comprises IRES site. Wickham et al teach adenoviral vectors comprising HB-EGF, 2a site and GFP. Wickham et al do not teach that the vectors comprise IRES site. However, Sosnowski et al teach viral vectors with modified tropism. The reference teaches adenovirus vectors comprising a targeting ligand. The reference teaches that the targeting ligand can be heparin binding growth factors, and heparin binding EGF like factor (HBEGF) (refers to the nucleic acid encoding HBEGF of the instant claims) (e.g., see column 11, column 22). The reference teaches heparin-binding epidermal growth factors (HBEGF) and DNA encoding HBEGF (e.g., see column 28). The reference teaches that the DNA sequence of the ligand is generally introduced into a plasmid in operative linkage with an appropriate promoter (refers to the promoter of interest of the instant claims) (e.g., see column 46). Sosnowski et al teach adenovirus vector comprising a nucleic acid molecule encoding a therapeutic gene product under control of a promoter (i.e., see column 3). The reference teaches that elements that increase the expression of the desired product are incorporated into the construct, and such elements include internal ribosome binding site (IRES of the instant claims) (e.g., see column 49). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use IRES site in the expression vectors such that the expression of the desired product is increased.

Response to Arguments

17. Applicant's arguments filed on 5/12/05 have been fully considered but they are not persuasive.

Claims 13, 15, 16, 17, 19, 20, 30, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,465,253 B1 (Wickham et al) and US patent 6,613,563 B1 (Sosnowski et al).

The instant claim 13 recites an expression vector comprising a nucleic acid encoding HBEGF, GFP and IRES.

Wickham et al teach vectors and methods for gene transfer to cells. The reference teaches modified adenovirus vectors comprising non-native amino acid sequences. The reference teaches non-native amino acid sequence of UTV or Universal Transfer Vector sequences. The reference preferably teaches the non-native amino acid sequence or UTV sequence comprises heparin binding motifs, and a stretch of 21 amino acids of the heparin binding epidermal growth factor like growth factor (HB-EGF) (refers to the HBEGF of the instant claims). The reference teaches adenoviral vectors, which can comprise additional sequences, a protease recognition sequence (refers to 2a site of the instant claims) (e.g., see column 17). The reference teaches that the vectors comprise additional marker genes such as gene encoding GFP (refers to the second selection gene or GFP of the instant claims) (e.g., see column 19). The reference teaches that the non-coding sequences include promoter sequences.

The claimed invention differs from the prior art teachings by reciting that the expression vector comprises IRES site. Wickham et al teach adenoviral vectors comprising HB-EGF, 2a site and GFP. Wickham et al do not teach that the vectors comprise IRES site. However, Sosnowski et al teach viral vectors with modified tropism. The reference teaches adenovirus vectors comprising a targeting ligand. The reference teaches that the targeting ligand can be heparin binding growth factors, and heparin binding EGF like factor (HBEGF) (refers to the nucleic acid encoding HBEGF of the instant claims) (e.g., see column 11, column 22). The reference teaches heparin-binding epidermal growth factors (HBEGF) and DNA encoding HBEGF (e.g., see column 28). The reference teaches that the DNA sequence of the ligand is generally introduced into a plasmid in operative linkage with an appropriate promoter (refers to the promoter of interest of the instant claims) (e.g., see column 46). The reference teaches that elements that increase the expression of the desired product are incorporated into the construct, and such elements

include internal ribosome binding site (IRES of the instant claims) (e.g., see column 49). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use IRES site in the expression vectors such that the expression of the desired product is increased.

The instant amended claims recite 'a promoter of interest.' Wikham et al teach that the expression vectors comprise a promoter which operably linked to the coding sequences (i.e., see columns 15, 16). Sosnowski et al teach adenovirus vector comprising a nucleic acid molecule encoding a therapeutic gene product under control of a promoter (i.e., see column 3).

Applicants traverse the rejection. Applicants argue that the examiner has not set forth any motivation to combine the references.

Applicant's arguments have been considered and are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, both the references (US Patent 6,465,253 (Wickham et al) and US Patent 6,613,563 (Sosnowski et al)) teach adenovirus vectors, and the targeting ligand HBEGF, and Snowsuit et al teach the advantages of the use of the IRES sites with adenoviral vectors. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use IRES site in the adenoviral vectors.

Applicants further argue the references individually. Applicants argue that Wickham et al reference does not disclose the vectors with protease site, and the reference only teaches it may

be present. And applicants argue that the reference discloses that instead of a therapeutic gene, the vectors may be used to transfer a marker gene such as GFP.

Applicants argue that Sosnowski et al do not teach 2a site, and the reference does not teach the use of IRES site with any other types of vectors.

Applicant's arguments regarding the teachings of Wickham et al and Sosnowski et al have been considered and are not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Wickham et al reference teaches all the instant independent claim limitations 'an expression vector comprising: a) a promoter of interest, b) nucleic acid encoding HBEGF, c) nucleic acid encoding GFP, except IRES. Wickham et al teach adenoviral expression vectors, and does not teach expression vectors with IRES site. However, Sosnowski et al teach adenoviral vectors with IRES site, and the advantages of the use of IRES sites with expression vectors.

Applicants further argue that Sosnowski et al teach gene therapy vectors and the design of gene expression vectors for gene transfer is an unpredictable art that is not always successful. Applicants further argue that there is no teaching or suggestion that the IRES site should be used in any other type of vectors.

Applicant's arguments are considered and are not persuasive. Applicant's arguments regarding unpredictable art are moot, because the instant claims are not drawn to gene therapy vectors or gene therapy method. And further Applicants arguments that the reference does not

teach the presence of IRES in any other vectors is not persuasive, since both the references are teaching adenoviral vectors, and further the instant claimed vectors are not limited any one single specific vectors.

Applicant's arguments regarding 'the use of IRES of the tropism modified vector in any other type of vectors' have been considered and are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the use of IRES in vectors in which tropism is not modified) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, for the reasons of record the rejection has been maintained.

Conclusion

18. No claims are allowed.

19. Claims 18, 26-27, 29, 33-37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PADMASHRI PONNALURI
PRIMARY EXAMINER

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

18 July 2005